UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/302,217	04/29/99	KELLER R	4250-2

HM12/0815

RONALD R SANTUCCI
KANE DALSIMER SULLIVAN KURUCZ LEVY
EISELE AND RICHARD LLP
20TH FLOOR - 711 THIRD AVENUE
NEW YORK NY 10017

EXAMINER	
TU,S	
ART UNIT	**PAPER NUMBER**
1653	4

DATE MAILED: 08/15/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/302,217	Applicant(s) KELLER ET AL.	
	Examiner Stephen Tu	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 101 — w/draw in view of arguments

1. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

2. Claims 6-18 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

review spec → w/draw in view of arg. & remainder of spec.

4. Claims 9-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the stimulation of glutathione production, does not reasonably provide enablement for shifting T-cell balance in allergy sufferers, reducing levels of serum cholesterol and triglycerides, decreasing fatigue, minimizing the effects of stress, or increasing energy in a mammal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, are set forth in *In re Wands*, 8 USPQ2d 1400, at

1404 (CAFC, 1988). These factors include: (1) the nature of the invention, (2) the state of the prior art, (3) the relative level of skill of those in the art, (4) the predictability of the art, (5) the breadth of the claims, (6) the amount of direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary.

The specification discloses that the administration of N-acetylcysteine has been shown to stimulate the natural production of glutathione, and this property has been demonstrated in the prior art. However, no such evidence is given or referred to that would support the assertion that the composition claimed is capable of shifting T-cell balance in allergy sufferers, reducing levels of serum cholesterol and triglycerides, decreasing fatigue, minimizing the effects of stress, or increasing energy in a mammal. Applicants state that their own studies indicate that the claimed compound is effective for these additional properties. However, no evidence is provided to support this assertion.

These additional properties affect very different biological processes. It is not evident from the prior art or from the specification that this composition would be equally effective in the treatment of these conditions. Nor is it evident that the prior art supports the correlation of increased glutathione production with shifting T-cell balance, reducing serum cholesterol and triglyceride levels, decreasing fatigue, minimizing the effects of stress, or increasing energy in a mammal. One of ordinary skill in the art would, therefore, not expect such correlation. Different dosages and formulations of the compound would be expected in addressing the appropriate treatment of these conditions. However, the specification does not provide any indication of the particulars of how the composition is to be used in treating these various conditions.

In the absence of any working examples or guidance on the use of this composition in shifting T-cell balance in allergy sufferers, reducing serum cholesterol and triglyceride levels, decreasing fatigue, minimizing the effects of stress, or increasing energy in a mammal, it is the position of the Examiner that undue experimentation would be required by one of ordinary skill in the art o practice the invention with respect to the treatment of these conditions. Specifically, one of ordinary skill in the art would have to determine not only how the compounds should be used but also the extent to which the compounds can be used. Otherwise, the activity of the composition, in addition to its ability to increase glutathione production, should be described in the specification.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

maintain b/c not sure how product is admin.?

6. Claims 6-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The recitation of "systemic administration" in these claims appears to provide for the use of a composition, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Δ → obl → route request to spell TH2, TH1 out & IgE

7. Claim 9 is rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites the acronyms "TH2" "TH1" and "TgE" but does not provide a definition for these acronyms. Applicant should

make the intended meaning of the acronyms clear by spelling out the term at its first instance and introducing the acronym in parentheses following the term.

1. Claims 15 and 16 are rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite "...wherein a pharmaceutically effective is...." While it appears that Applicants intend to recite "a pharmaceutically effective amount", however, Applicant should make this explicit and unambiguous. Appropriate correction is required.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 2, 6, and 15-18 are rejected under 35 U.S.C. 102(b) as being anticipated by BIODYNAMAX, BioDynamax Supplement – Ultra Antioxidants Tablets, Product Alert (22 Dec 1997). BIODYNAMAX discloses N-acetylcysteine in an admixture with Vitamin C, milk thistle (sylimarin), quercetin, and α-lipoic acid. The composition has been formulated as a dietary supplement of antioxidants, thus it is clearly intended for human consumption. The reference also states that the composition provides "the most comprehensive antioxidant protection in one convenient formula."

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-3, 5-8, and 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over BIODYNAMAX, BioDynamax Supplement – Ultra Antioxidants Tablets, Product Alert (22 Dec 1997) and KAMINSKI et al., Alternative Medicine Review (1998) 3(1):40-53.

BIODYNAMAX is applied as cited in the above rejection. The reference teaches a mixture of N-acetylcysteine with Vitamin C, milk thistle (sylimarin), quercetin, and α-lipoic acid. However, BIODYNAMAX does not teach the administration of this composition with glutamine, probiotics or flavorants. This reference also fails to disclose the use of the composition as a treatment for hepatitis.

KAMINSKI et al., on the other hand, teaches that N-acetylcysteine and α-lipoic acid inhibits the expression of TNF-α and NF-κB (see page 45). The overexpression of TNF- α in individuals infected with HIV induces increased oxidative stress (see page 43). Antioxidants such as N-acetylcysteine and α-lipoic acid are safe, non-toxic compounds that can be administered to mitigate the effects of oxidative stress in individuals infected with HIV. The

reference also teaches that glutamine and probiotics can also be administered to maintain the appropriate balance of beneficial intestinal bacteria to minimize vulnerability to enteropathogens (see p. 48). In addition, KAMINSKI et al. also teaches that administration of glutamine helps to alleviate Phase I and II detoxification problems in instances of hepatic inflammation (see p. 49).

With respect to the addition of flavorants, it is a matter of routine practice to use a flavorant to make a pharmaceutical composition more palatable, particularly where the flavor or taste of the composition, without a flavorant, would be considered objectionable. Thus, the addition of a flavorant would have been readily apparent to one of ordinary skill in the art, especially if the flavor of this composition is of concern.

Thus it would have been obvious to one of ordinary skill in the art at the time the invention was made to have combined the teachings of KAMINSKI with BIODYNAMAX to prepare a composition that would mitigate the effects of oxidative stress in HIV infected individuals.

7. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over BIODYNAMAX and KAMINSKI et al. as applied to claims 1-3, 5-8, and 15-18 above, and further in view of BOUNOUS et al., US 5,290,571.

BIODYNAMAX and KAMINSKI et al. are applied as cited in the above rejection. Neither of these references teach the administration of the N-acetylcysteine together with a dietary protein. Applicants have stated, in their specification, that one example of a suitable dietary protein is an undenatured whey concentrate (see Specification, page 11).

BOUNOUS et al. teaches that immune response is enhanced in mice that were fed whey protein concentrate as a result of the increased production of splenic glutathione. The reference

also teaches that the efficiency of dietary cysteine in inducing increased glutathione production is higher when it is delivered in whey protein (see column 4, lines 39-47).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of KAMINSKI and BIODYNAMAX with BOUNOUS et al. to prepare a composition that enhances the efficiency of dietary delivery of cysteine in order to induce increased glutathione production.

No claims are allowed.

Please note that with regard to the rejection of Claims 1, 2, 6, and 15-18 under 102(b), BOUNOUS et al. shows that supplementing various forms of cysteine, in particular N-acetylcysteine, can increase cellular levels of glutathione by stimulating the production of glutathione. The reference is not relied upon in this rejection, rather it is cited only to demonstrate what was known in the art at that time (see column 3, lines 30 – 66).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Tu whose telephone number is 703-308-3968. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 703-308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ST
August 14, 2000

Christopher S. F. Low

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600